Given early in the morning in warm water, they lend effective aid to the operation of the mixtures already mentioned.

In what I have said I have given from individual experience. There are some physicians who advocate the use of caustics, such as sulphate of copper and nitrate of silver. There are others who advocate the use of opium and astringents; but all I can do is to tell what, in no inconsiderable experience, has appeared to me to be the most effective mode of treatment.

I should like to add a few words on the value of iodide of potassium in the treatment of gastric catarrh, whether simple, or complicating ulcer, or complicating malignant disease. Administered with the addition of some bicarbonate of potash or soda, it is, in my experience, a drug of inestimable value. It speedily removes a simple catarrh. It thereby removes the primary obstacle to the treatment of ulcer; and, in malignant disease, it will often, for a time, so far mitigate the symptoms as to make the patient think he is being cured. I have often found it in malignant disease relieve the patient for a time, and, I think, prolong life, with marked diminution of suffering.

It will be observed that I have dealt with gastric ulcer clinically, as I undertook. The subject of the diagnosis of gastric ulcer must be constantly in the mind of the practitioner of medicine. It has been much in my mind for years. And what I have put on record here, crude and elementary as it is, represents much careful thought and long observation.

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STUDIES ON THE ETIOLOGY OF THE PNEUMONIA COMPLICATING DIPHTHERIA IN CHILDREN.[1]

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AND

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The classification of the inflammations of the lungs has assumed a new phase since the improved methods of studying the bacteria have become definitely formulated and widely practised. While formerly morphological distinctions, either gross or minute, between the different forms of inflammation were ardently sought after and minutely detailed, the pathologist is now disposed, while still cherishing the approved morphological data, to seek for the etiological factors which more or less definitely determine the varying phases which inflammations of the lungs may assume, and upon these to base, at least, a provisional and supplementary working classification.

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[1] The statistical data on the frequency of the disease, the clinical history of the cases, and most of the children's lungs made use of in these studies have been furnished by Dr. Northrup. The microscopical and experimental work was done by Dr. Prudden.

Thus it has been found that that common and well-defined form of pulmonary inflammation called acute lobar pneumonia is, in a large proportion of cases at least, associated with and no doubt directly induced by the growth in the lungs, when the conditions are favorable, of a diplococcus known as the Diplococcus pneumoniæ of Fränkel and Weichselbaum. This bacterium, as appears from the researches of Sternberg, Fränkel, and others, is a not uncommon denizen of the mouths of healthy persons.

In the new etiological classification of inflammations of the lungs, then, acute lobar pneumonia is an inflammation usually induced by the Diplococcus pneumoniæ, and presenting in general those clinical gross and minute features which have long been known and frequently described. This form of pneumonia, while so frequently lobar in its extent and distribution as to justify its name, may, nevertheless, develop in various atypical ways, and occurring, as it sometimes does, in lobular form has still been found to be associated with the same bacteria. Whether in inciting this disease the bacteria always find access to the lungs through the upper air-passages, as seems most probable, or occasionally from the blood, we cannot yet positively say.

While, furthermore, it seems well established that the Diplococcus pneumoniæ is the most common primary bacterial etiological factor in the ordinary acute lobar pneumonia, it is not unlikely that some other forms of bacteria, particularly the pneumo-bacillus of Friedländer, may occasionally incite the disease and cause typical symptoms and lesions.

Another form of inflammation of the lungs, protean in its phases, is that which occurs directly or indirectly under the influence of the Bacillus tuberculosis. That the bacteria of tuberculosis, in a great many cases at least, gain access to the lungs with dust in the inspired air, is well established.

Still another form of pulmonary inflammation, as viewed from the etiological stand-point, is the so-called embolic pneumonia induced by the lodgement in the pulmonary bloodvessels and their subsequent growth in the lung tissue of bacteria, more commonly the pyogenic cocci, brought from some other part of the body.

In these well-defined forms of pulmonary inflammation the inciting species of bacteria have been identified by cultures over and over again by various observers, so that their nature as bacterial diseases may be regarded as well established. All of these inflammations are liable to be associated with bacteritic inflammations due to the same cause in various other parts of the body (1).

In sharp distinction to these bacteritic pneumonias stands a group of lesions, generally considered more or less loosely as inflammations, which, although sometimes remotely and secondarily, are never directly dependent upon the presence of bacteria in the lungs. Such are the chronic interstitial and intra-alveolar pneumonias, be they anthracotic or cardiac or syphilitic in origin, or due to trauma or some other local cause, such as foreign bodies, tumors, etc. We do not now speak of gummata of the lungs, of the relations of which to bacteria we are still in ignorance.

It is probable that the ordinary so-called hypostatic pneumonias are not regularly associated with the presence of bacteria. The part which bacteria play either primarily or secondarily in gangrene of the lungs is too little known to permit of a definite classification of its varying phases here. It seems hardly necessary to mention here that the lesions of the bacteritic and the non-bacteritic inflammations of the lungs are very frequently associated in the same individual.

While definite and positive researches by the improved culture methods have justified us in such a grouping as indicated above of certain of the more common bacteritic, in distinction from the non-bacteritic pneumonias, there is still a considerable number of phases of the inflammatory process in the lungs, especially those large and important groups known as the secondary lobar or lobular and broncho-pneumonias about the direct inciting cause of which we as yet know very little.

These phases of inflammation are apt to occur under a great variety of conditions as complications of other disorders. While we know a good deal about the conditions under which they most frequently occur, the bacterial studies upon them by the modern methods have been so few and so desultory that it is at present impossible to say definitely whether bacteria do or do not stand in a causative relation to many or most of them.

In acute lobar pneumonia, the clinical history, lesions, and complications of which are so well defined and typical, the presumption is decidedly against more than one species of bacteria being the common and ordinary inciting cause. On the other hand, in the lobular and broncho-pneumonias, both of adults and children, if they are bacterial in origin at all, the presumption appears rather in favor of the hypothesis that there may be many species of bacteria which may serve as the inciting cause of the lesion under different circumstances.

If we make a brief summary of the definite results which have been obtained by the bacterial studies on the secondary complicating lobular and broncho-pneumonias, rejecting for the most part the numerous simple morphological examinations, which are, from the nature of the case, always incomplete, and considering only those which by the culture methods have led to decisive results, we shall find that while a good beginning has been made, the observations are, on the whole, very incomplete.

That localized inflammations of the lungs may be induced by the presence of anthrax bacilli, by the bacillus of glanders, and by the actinomycosis is well established, though in man in this region these forms of pulmonary inflammation are not frequent enough to be of great practical importance.

There is a form of pneumonia which is a direct propagation of the inflammatory process from the pleura (pleurogenous pneumonia) and which has been proven to be due to the same organisms as those inciting the primary pleurisy.

There are, finally, some isolated observations, not sufficiently numerous and not fully enough controlled by the culture methods to be regarded as very significant, which would indicate the probability that now and then the Bacillus typhosis and the Streptococcus erysipelatos may, in the course of typhoid fever and erysipelas, obtain a foothold in the lung and induce a more or less extensive lobar or lobular inflammation (2).

In 1886 Weichselbaum (3), in his studies on various forms of acute pneumonia, found a streptococcus in eight cases of secondary pneumonia. Two of these were lobar and associated one with rheumatism and the other with senile gangrene of the leg. The others were lobular, and associated with erysipelas, phlegmonous inflammation of the nose and mouth, progressive paralysis, and nephritis. This streptococcus appeared to him on both morphological and biological grounds to be similar to the Streptococcus pyogenes and Streptococcus erysipelatos, though he does not positively declare his belief in their identity. He names it the Streptococcus pneumoniæ.

Neumann (4) has cultivated from the lungs in a case of simple bronchopneumonia the Staphylococcus pyogenes aureus and albus.

In 1887 Guarnier (5) found in the lungs of a child dead of bronchopneumonia after measles, by morphological and culture methods, a streptococcus apparently identical with the Streptococcus erysipelatos.

In connection with his studies on the etiology of diphtheria in 1884, Löffler (6) made morphological examinations of the lungs of several persons dead of diphtheria. In the typical hemorrhagic broncho-pneumonia of this disease he frequently found streptococci, and not the bacilli which he had found in the pseudo-membrane. As he made no cultures, however, from the lungs, these observations are not of great significance.

In 1885 Fränkel (7) cultivated from the lung in a case of bronchopneumonia complicating diphtheria in an adult, a streptococcus which seemed to him morphologically and biologically identical with Streptococcus pyogenes.

Experiments on the artificial induction of lobular and broncho-pneumonia in animals by the introduction of bacteria into the lungs have been made by several observers, and will be considered later in this paper.

It would thus appear from the scattered results which we have gleaned in the literature that the logical procedure in studying the etiology of the secondary lobular and broncho-pneumonias is not to make the attempt at first to investigate every form of the disease which comes to hand under the greatest variety of conditions, but rather to attempt the systematic study of certain well-defined groups or classes of the lesion. One of the best defined, as well as one of the most important of these groups, is the broncho-pneumonia which so frequently complicates measles and scarlatina and diphtheria in children.

In connection with recent studies by one of us on the etiology of diphtheria in children (8) we have made a series of observations and experiments on the broncho-pneumonia which so frequently complicates the disease which it is the purpose of this paper to record.

Frequency of the Occurrence of Broncho-pneumonia in Diphtheria.

Darier (9) in 181 autopsies upon patients dead of diphtheria found broncho-pneumonia in 61 cases.

Talamon (10) in 121 autopsies found broncho-pneumonia in 69 cases.

Schrakamp (11) in 54 autopsies found broncho-pneumonia in 31 cases.

In 195 autopsies upon children dead of diphtheria at the New York Foundling Asylum, well-marked, recent broncho-pneumonia was present in 133 cases.

If we reduce these data to percentages, we see that Darier found broncho-pneumonia in 34 per cent. of cases of fatal diphtheria, Talamon in 64 per cent., Schrakamp in 57 per cent., and Northrup in 68 per cent. On the whole, then, we may say that so far as these statistics go, broncho-pneumonia is present in fatal diphtheria, as a complication, in about 55 per cent. of the cases.

These data, however, have but a limited significance, since a careful microscopical examination of the lungs of children dead with diphtheria of the air-passages shows that there may actually be a considerable amount of lobular inflammation without gross change. Thus, in the 195 New York Foundling Asylum cases there was a considerable number of lungs in which there were areas of localized congestion or hemorrhage or collapse, which a microscopical examination might have shown to be associated with slight inflammatory changes, but which, owing to the uncertainty, were not counted among the pneumonias. This condition of affairs would seem to indicate that the above percentage is low rather than high.

SEVENTEEN CASES OF DIPHTHERITIC BRONCHO-PNEUMONIA EXAMINED.

These cases have been described more fully in the paper on diphtheria above referred to, so that here only those details are given which bear directly on the subject in hand. But it should be borne in mind that, as already recorded, cultures as well as microscopical examinations were made of the pseudo-membranes in all of them, and the Streptococcus diphtheriæ was found, usually in large numbers, in all except Case XIV.

Cases I. to XIV., inclusive, were from the New York Foundling Asylum. Cases XV. and XVI. were from the Randall's Island Infant Asylum. Case XVII. from private practice.

CASE I.—Male, three years two months. Diphtheria following rectal abscess; death on fifth day. Autopsy: Voluminous firm pseudo-membrane in larynx, trachea, and larger bronchi. Moderate amount of broncho-pneumonia, with large involvement of bronchi. *Bacterial examination of lungs:* Small numbers of cocci and diplococci in bronchial exudate as well as in the air-spaces. *Cultures* showed large number of *streptococci;* a few Staphylococcus pyogenes aureus and a few stout, round-end bacilli with scattering forms.

CASE II.—Male, seven months. Diphtheria following pertussis; death on fourth day. Autopsy: Moderate amount of pseudo-membrane in trachea and larger bronchi; this in the bronchi was much softened. Broncho-pneumonia, involving right lower and part of middle lobe. *Bacterial examination of lungs:* Large numbers of cocci in bronchial exudation, and enormous numbers, single and in chains, in exudation in air-vesicles. *Cultures* show vast numbers of *streptococci* and a few Staphylococcus pyogenes aureus.

CASE III.—Female, two and one-half years. Diphtheria; death on seventh day. Autopsy: Pseudo-membrane in pharynx, larynx, and trachea; old and fresh broncho pneumonia in both lower lobes posteriorly. *Bacterial examination of lungs:* In areas of old broncho-pneumonia no bacteria were found. In the fresh bronchial exudation, as well as in areas of fresh and commencing consolidation, enormous numbers of cocci, single, paired, and in chains. *Cultures* from areas of fresh broncho-pneumonia showed great numbers of *streptococcus* colonies and a few of Staphylococcus pyogenes aureus.

CASE IV.—Male, three years. Diphtheria following pertussis, with albuminuria and broncho-pneumonia on third and fourth day; death on eighteenth day after commencement of pertussis. Autopsy: Softened membrane in large and small bronchi, with considerable old and moderate amount of fresh broncho-pneumonia. *Bacterial examination of lungs:* No bacteria found in areas of old consolidation. In the bronchial exudate, as well as in the areas of fresh consolidation, large numbers of cocci, single, double, and in chains, with a few scattering forms. *Cultures* show large numbers of *streptococci* from bronchial exudate and from areas of fresh consolidation; also a few Staphylococcus pyogenes aureus.

CASE V.—Young child. Diphtheria, followed by broncho-pneumonia, accompanied by umbilical phlegmon. Autopsy: Voluminous membrane n larynx, trachea, and bronchi; congestion and broncho-pneumonia in both lower lobes. *Bacterial examination of lungs:* Enormous numbers of cocci, single, paired, and in chains, in bronchial exudation and in contents of air-vesicles in consolidated areas. *Cultures* show vast number of *streptococci* and considerable number of Staphylococcus pyogenes aureus.

CASE VI.—Young child. Diphtheria, followed by broncho pneumonia. Autopsy: Moderate amount of pseudo-membrane, very slight amount of fresh broncho-pneumonia, considerable amount of old broncho-pneumonia. *Bacterial examination of lungs:* In bronchial exudation few cocci and scattering bacilli; very few cocci in areas of commencing consolidation in lungs. *Cultures* show moderate number of colonies of *streptococci*, considerable number of Staphylococcus pyogenes aureus, and many stout bacilli.

CASE VII.—Young child. Diphtheria with umbilical phlegmon. Autopsy: Pseudo-membrane in larynx, pharynx, and trachea, loosening and softening below. Considerable amount of fresh broncho-pneumonia in both lower lobes. *Bacterial examination of lungs:* In exudation in air spaces, largely made up of red blood-cells, enormous numbers of streptococci. *Cultures* show large numbers of *streptococci*, Staphylococci pyogenes aureus, and a considerable number of scattering forms.

CASE VIII.—Female, three years eight months. Diphtheria following measles; death on sixth day. Autopsy: Softening membrane in trachea, extending into bronchi. Both posterior lower lobes red and mottled with solid areas. *Bacterial examination of lungs:* Considerable atelectasis with a little exudation in scattered regions. The smaller bronchi in the affected regions are filled with pus-cells, and desquamated epithelium, mingled with a large number of cocci, single, paired, and in chains. In the air-spaces adjacent and belonging to these affected bronchi the air-vesicles are filled with cellular and granular exudation, intermingled with cocci, single and in chains. *Cultures* show large numbers of *streptococci*, with a few Staphylococcus pyogenes aureus and some scattering forms.

CASE IX.—Male, two and one-half years. Diphtheria; death on eighth day. Autopsy: Pseudo membrane in pharynx and larynx; no broncho-pneumonia evident to the naked eye. *Bacterial examination of the lungs:* Acute bronchitis with considerable exudation in some of the smaller bronchi. Large numbers of streptococci mingled with the exudation in the lumen of the inflamed bronchi. In the bronchioles, air passages, and air-vesicles nearest to the inflamed bronchi and belonging to the same systems were enormous numbers of streptococci and single cocci. In the air-vesicles a few desquamated epithelial and pus-cells and granular material were intermingled with the bacteria. In this case we seem to have a very early stage of the broncho-pneumonic process. *Cultures* show considerable numbers of *streptococci* and a few scattering forms of bacilli.

CASE X.—Female, one year. Diphtheria of pharynx and tonsils; enterocolitis; death on third day. Autopsy: Small amount of firm pseudo-membrane on pharynx, tonsils, and at the upper end of œsophagus. Both posterior lower lobes of the lungs show congestion and a moderate amount of scattered lobular consolidation. *Bacterial examination of lungs:* Consolidated areas in the lungs are mostly due to old broncho-pneumonia with much exudation in the smaller bronchi. In fresh exudation a few cocci were found intermingled with the cells, while in the areas of old consolidation none were discovered. *Cultures* from the redder areas of pneumonia showed a few *streptococci*, a few Staphylococcus pyogenes aureus and albus, and some scattering forms.

CASE XI.—Female, two years. Broncho-pneumonia with apparent recovery, followed by diphtheria of the pharynx and fresh broncho-pneumonia, with death on second day. Autopsy: Irregular consolidation of the left lower lobe with congestion. *Bacterial examination of lungs:* The broncho-pneumonia was found to be largely old, but in places the exudation was fresh, accompanied by considerable congestion. In the areas of old consolidation no bacteria were found. In the air-spaces containing the fresh exudation a considerable number of streptococcus chains were found. *Cultures* from the lungs showed large numbers of *streptococci*, a considerable number of Staphylococci pyogenes aureus, and a few scattering forms.

CASE XII.—Male, three years. Diphtheria following scarlatina, tubercular peritonitis; small patch of pseudo-membrane at the base of the tongue and in the larynx and trachea; softening below. Autopsy: Both lungs showed scattered areas of congestion and partial consolidation. *Bacterial examination of lungs:* Microscopical examination of the lung showed that the consolidated areas were in large part due to the old pneumonia, while in the congested parts there was a moderate amount of fresh exudation and enormous numbers of streptococci, often forming large masses of snarls or chains. *Cultures* from pneumonic areas in both lungs showed vast numbers of *streptococci*, considerable numbers of Staphylococcus pyogenes aureus and albus, with a few stout bacilli.

CASE XIII.—Diphtheria, with death on third day. Autopsy: Pseudo-membrane in the pharynx, larynx, trachea, and bronchi; firm and voluminous. Moderate amount of consolidation in both lower lobes of the lungs. *Bacterial examination of lungs:* Very few scattering cocci were found in consolidated areas and in bronchial exudation. *Cultures* of consolidated areas in the lung show a large number of *streptococci* (pure culture).

CASE XIV.—Male, three and one-half years. Enterocolitis, diphtheria, intubation; death on third day. Autopsy: Moderately firm pseudo-membrane in the larynx; small amount of broncho-pneumonia in both lower lobes. *Bacterial examination of lungs:* Moderate amount of exudation in spots in the lungs, but only a very few scattering forms of bacteria, mostly stout bacilli. *Cultures* from the lungs showed considerable numbers of *streptococci*, and only a very few scattering forms.

CASE XV.—Diphtheria following measles; death on seventh day. Autopsy: pseudo-membrane in larynx and trachea; tubercular bronchial glands; consolidation of both lower lobes of the lungs; pleurisy. *Bacterial examination of lungs:* Considerable old broncho-pneumonia. In new exudation a moderate number of cocci. In areas of old broncho-pneumonia no bacteria were found. *Cultures* of the lungs show a large number of *streptococcus* colonies, a few of Staphylococcus pyogenes aureus, and scattering forms.

CASE XVI.—Diphtheria following measles; death in twenty-four hours. Autopsy: No pseudo-membrane; commencing broncho-pneumonia. *Bacterial examination of lungs:* Moderate number of cocci, single and in chains, in the exudation. *Cultures* show many *streptococcus* colonies and a few scattering forms.

CASE XVII.—Female, two and one-half years. Diphtheria with early development of constitutional symptoms, tracheotomy, death. Autopsy:

Voluminous pseudo-membrane in trachea; slight broncho-pneumonia. *Bacterial examination of lungs:* Microscopical examination not made, the lungs being destroyed by mistake after the cultures were started. *Cultures* of pneumonic areas of the lungs show large numbers of *streptococcus* colonies and besides these only a few scattering forms.

SUMMARY OF EXAMINATIONS AND CULTURES FROM DIPHTHERITIC BRONCHO PNEUMONIA CASES.

We thus see that the areas of fresh broncho-pneumonia in the lungs of seventeen young children, dead of diphtheria, showed, with one exception, the presence of considerable or large numbers of streptococci. The exceptional case was one in which no streptococci were found in the pseudo-membranes. The streptococcus was the only form present in the pneumonic areas with such uniformity and in such abundance as to appear of significance. The streptococci isolated from the lungs in these cases present exactly the same morphological, biological, and pathogenic characters as those of the streptococci found in the pseudo-membranes from the same cases, and which have already been described and called Streptococcus diphtheriæ (8).

The reason for believing these bacteria to be identical with the Streptococcus pyogenes and Streptococcus erysipelatos are set forth in the paper above referred to.

CONTROL CASES.

NON-DIPHTHERITIC BRONCHO-PNEUMONIA.—For purposes of control I have made cultures from the consolidated areas in the lobular and broncho-pneumonia of young children, not associated with diphtheria (10 cases). In two of the cases the pneumonia occurred with whooping-cough, in one with erysipelas, in two with marasmus, in five without any other apparent complication. In only a few of these ten cases have I found either by microscopical examination or by cultures any species of bacteria in considerable numbers, nor were the same species found in the different cases with sufficient frequency to indicate that, whether abundant or not, they were of special significance. Thus in two of the cases there were in the pneumonic areas many of the short bacilli which are common in the mouths of children, and which I have called chain-bacilli, and in four of the cases there were very small numbers of Streptococcus pyogenes aureus. The streptococcus was found in only one of these cases.

This exceptional case, the only one out of ten of non-diphtheritic broncho-pneumonia examined in which streptococci, both by culture and microscopical examination, were shown to be present in the lungs, was the above-mentioned case of erysipelas. In this case, however, although the cultures showed large numbers of streptococci in the lungs as well as in the skin, liver, kidney, and spleen, in the lungs the bacteria were only found in the bloodvessels, and never in the exudation in the bronchi or air-spaces. In this case, then, there was a general infection through the bloodvessels with erysipelas streptococci, and, although present in the bloodvessels of the lungs, they apparently have no relation either in situation or in numbers to the slight amount of broncho pneumonia present.

ACUTE LOBAR PNEUMONIA.—Furthermore, I have made cultures from three cases of typical acute lobar pneumonia in children between two and three years old. These children all died at an early period in the disease, and from the consolidated areas in all of them I cultivated enormous numbers of the pneumococcus of Fränkel and Weichselbaum. In addition to this species, in one of the cases there were large numbers, in another a few, of the Staphylococcus pyogenes aureus. Besides these there were only scattering forms. No streptococci were found in these cases.

NORMAL LUNGS.—Finally, I have made cultures from lungs, apparently normal, taken from the bodies of children dead of enterocolitis (two cases), marasmus (three cases). In none of these lungs have I found, either microscopically or by cultures, streptococci. In two of the cases of marasmus, the common fluidifying fluorescent bacillus of water was present in considerable numbers, and in the others only a few scattering forms.

SUMMARY OF CULTURES IN THE CONTROL CASES.

In ten cases of lobular and broncho-pneumonia in children not diphtheritic, in three cases of typical acute lobar pneumonia in young children, and in five cases dead of enterocolitis or marasmus with apparently healthy lungs (eighteen cases in all), the cultures of the lungs showed no streptococci, except in one case of erysipelas with general systemic infection; in six a few Staphylococcus pyogenes aureus were present. Besides, there were a few scattering forms, mostly short, stout bacilli, in the various cases.

GENERAL SUMMARY OF CULTURES IN ALL THE CASES.

We thus see that streptococci were present in large numbers in the freshly affected lobular and broncho-pneumonic areas of children suffering from diphtheria in fifteen out of sixteen cases; while in the lungs either normal or pneumonic of eighteen non-diphtheritic children placed under the same sanitary conditions no streptococci were found except in the bloodvessels of a case of erysipelas with general infection.

HISTOLOGICAL DETAILS.

In recording the results of the morphological and biological examination of the lungs in these seventeen cases of pneumonia associated with diphtheria, and placing them in contrast with similar results obtained from the lungs in non diphtheritic cases, it has seemed wise to give only a succinct statement of the facts elicited. Some histological data have, however, been developed in the various examinations which are not without significance in connection with the general subject of lobular and broncho-pneumonia in young children.

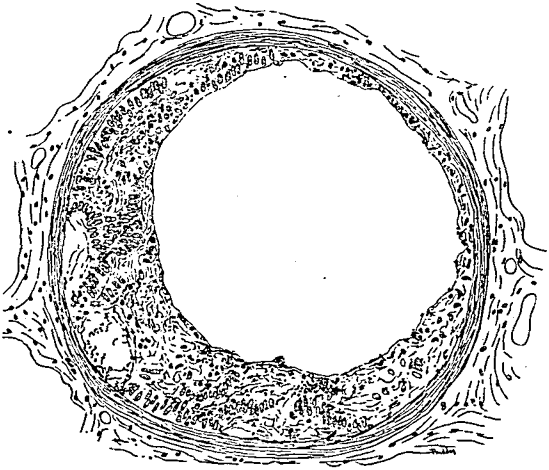
In the first place, in many of the control cases of simple lobular and broncho-pneumonia, of which that subacute or chronic form which is so common in marasmus children may be regarded as typical, neither by cultures nor by morphological examinations can we find evidence that bacteria are present or have anything to do with the lesions. In this form of pneumonia the bloodvessels in the affected regions are apt to be dilated, the walls of both bronchi and air-spaces more or less thickened, and often infiltrated with cells. While the air-spaces contain sometimes a few, sometimes many, large cells, which seem to be desquamated alveolar epithelium, neither blood nor fibrin nor pus is commonly present. This form of pneumonia sometimes is and sometimes is not associated with atelectasis. It appears to correspond in its general nature to some forms of hypostatic pneumonia in adults. Now, in many of our cases of diphtheria occurring in the New York Foundling Asylum this form of lesion was the prominent, and in many of the early fatal cases, was the only lesion evident in the gross examination.

On the other hand, I have found in the lungs of nearly all of the diphtheritic children, sometimes with and sometimes without the above form of lesion, an entirely different type of inflammation. In this inflammation in its well-marked phases there sometimes is and sometimes is not congestion of the bloodvessels in the affected regions. The smaller bronchi are apt to be more or less blocked with pus cells, and the air-spaces to contain in varying amounts pus-cells, red blood-cells, fibrin, granular material, desquamated epithelium, and bacteria. The bacteria in our cases were almost exclusively cocci, and the larger proportion of these were arranged in streptococcus form. These bacteria did not appear to be generally enclosed in the exudation cells, though often clustered close about them; nor were they often found in the walls of the air spaces, but they lay free in the exudation mass or were clinging to the walls of the vesicles. They were present sometimes in very small numbers, but often in enormous quantities.

Not infrequently only a few small areas in the lungs were involved in this way, and these were more frequently in the posterior portions. When markedly hemorrhagic in character, so that the air-spaces contain large numbers of red blood-cells, the involved areas in the gross examination of the lungs appear like areas of localized intense congestion, but they are apt to be lobular in distribution. Atelectasis was rarely observed in the regions involved in this form of pneumonia.

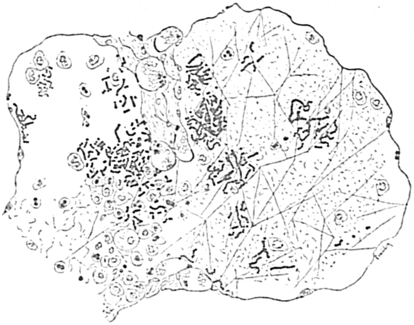
While in the main there is such a degree of inflammation in the

PLATE I.



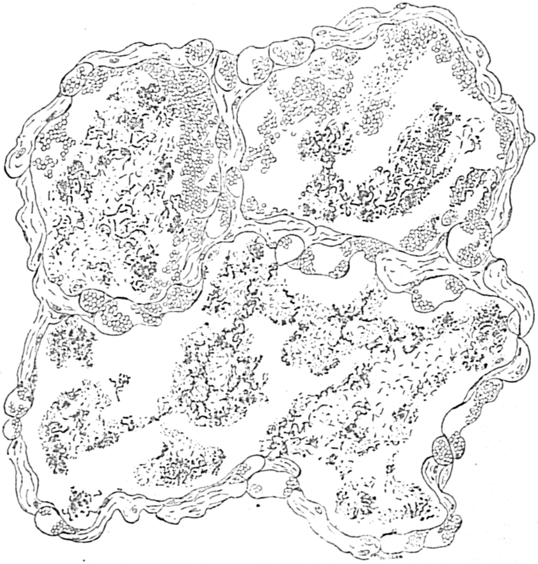
Small branches from Case IX. Showing exudation with streptococci.

PLATE II.—FIG. 1.



Two adjacent air-vesicles from CASE V. Showing exudation consisting of fibrine, leucocytes, and epithelium, intermingled with streptococci. (The bacteria are drawn proportionally a little too large.)

FIG. 2.



Hemorrhagic form of lobular pneumonia, CASE VII. Intermingled with the red blood cells and granular material in the air vesicles are large numbers of streptococci.

smaller bronchi as to render the designation of broncho-pneumonia applicable to the lesion, there are apt to be in most of the lungs areas of consolidation in which no change in the bronchi can be made out. Such areas of simple lobular inflammation may constitute the entire lesion in some lungs without any participation of the bronchi.

The distribution and general characters of this lesion, whether involving the bronchi or not, would seem to indicate that it is a form of inspiration pneumonia, "Schluck-pneumonie" of the Germans. This view is sustained by the observation that it was apt to be most marked and highly developed in children which had died after the pseudo-membranes in the air-passages above had begun to soften and break down.

Not infrequently one encounters in these lungs larger and smaller areas of consolidation in which the exudation is exactly of the same character as that just described, and indicative of an acute inflammatory process, but in which bacteria are entirely absent or, at least, not to be observed by any of the various means commonly resorted to. The explanation of this condition will be seen when we come to the results of animal experiments.

A very marked feature of this form of secondary broncho- or lobular pneumonia with diphtheria is the hyperplasia of the lymph nodes and nodules in and about the lungs. Not only are the larger and smaller bronchial lymph nodes (lymph glands) usually greatly enlarged, but the minute islets of lymphatic tissue (lymph nodules) which are scattered about the lungs in the interstitial tissue, as described by Arnold, are, especially in and near areas of inflammation, so large as to form prominent features in the microscopical sections.

Some of the varying phases of this form of pneumonia and the relation of the tissue to the streptococci are shown in the plates.

In Plate I. is represented a small bronchus from Case IX., in which the epithelium is nearly all detached and, together with mucus, a few pus-cells, and streptococci, forms an exudation mass partially filling the lumen of the tube. The air-vesicles adjacent to this bronchus and belonging to its system of air-spaces contained large numbers of pus and epithelial cells intermingled with streptococci.

Plate II., Fig. 1, shows two adjacent air-vesicles in consolidated areas of the lungs of Case V. In one of these vesicles the inflammatory exudate is largely fibrinous, while in the other there are epithelial and pus-cells. In both the streptoccoci are present in considerable numbers.

Plate II., Fig. 2, shows three adjacent air-vesicles from the lungs in Case VII., in which the exudate is largely made up of red blood-cells and granular material. Here the streptococci are present in very large numbers.

It should be mentioned here as bearing upon the theme of this paper, that the air of the New York Foundling Asylum while these researches were in progress, was usually found to contain the Staphylococcus pyogenes aureus and albus, and in one analysis the streptococcus floated with the dust. Furthermore, the bacterial examination of the scrapings of the mouths and throats of children, both sick and well, who were inmates of the asylum showed that the Staphylococcus pyogenes aureus was frequently present in those situations in considerable numbers. While the Staphylococcus pyogenes was present in the lungs in a considerable number of the cases of broncho-pneumonia with diphtheria, the lack of uniformity in its occurrence and the small numbers in which it was usually found, coupled with its frequent occurrence in the air and in the mouths of healthy children, would lead us to infer that its presence in the lungs in these cases is of but doubtful significance.

Our observations thus far, then, would seem to justify us in the hypothesis that if the acute broncho-pneumonia which accompanied the diphtheria in the cases which we have examined was bacterial in origin at all, it was probably due to the entrance into the lungs through the bronchi from the local lesion above of the Streptococcus diphtheriæ. But plausible as this hypothesis appears to be, it is necessary to have recourse to animal experiments in order to complete its demonstration. To these let us now turn our attention.

ANIMAL EXPERIMENTS.

A good deal of experimental work has been done in the artificial production of lobular and broncho-pneumonia in animals, either by the introduction of irritating vapors or fluids or solids directly into the lungs through the trachea, or by causing the entrance into the air-passages of fluids and solids from the mouth as the result of section of the vagus nerves. To the results of these experiments I need only thus briefly refer, since our theme is limited in scope to the introduction of pure cultures of known forms of bacteria.

I have used in these experiments, which were done exclusively on rabbits, cultures of the streptococci obtained from the lungs of five of the above described cases of diphtheritic broncho-pneumonia. Actively growing beef-tea cultures from two to five days old were used.

Preliminary experiments have shown that the introduction of the streptococcus directly into the lung by a puncture of the thoracic wall, is usually followed by fibrinous pleurisy and localized inflammation of the lung about the point of puncture. But the conditions of infection in this way are so much more complex and so unlike those under which the broncho- and lobular pneumonia of diphtheria in children occurs that the details of my experiments in this direction need not be given here.

INJECTIONS OF THE STREPTOCOCCUS DIPHTHERIÆ INTO THE LUNGS OF RABBITS THROUGH THE TRACHEA.—The mode of procedure in these experiments was to sterilize carefully the skin about the neck, after cutting away the hair, and then having made a small incision, exposing the trachea, to thrust the needle of the injecting syringe through its walls. From one to five c.c. of the beef-tea culture was injected, the small wound washed with sublimate or carbolic solution and bound up. The animals were held upright for a few moments after the injection in order to allow the fluid to run down into the lungs. Usually there was little or no local inflammatory reaction at the point of operation in the neck. Fifteen rabbits were operated upon in this way.

In most cases immediately after the injection coarse râles were heard over the thorax of the animals and in about one-third of the cases there was marked dyspnœa. Three of the animals with symptoms of increasing dyspnœa, loss of appetite, and progressive weakness, died, two on the second and one on the third day after the operation. The remaining animals appeared to recover rapidly from the initiatory dyspnœa, and afterward showed no sign of illness. These were killed at intervals of from three and one-half hours to ten days.

In seven of the fifteen cases no gross lesions were seen in the lungs. In the remaining cases there were larger or smaller areas of localized consolidation and congestion grouped in lobular form about the larger and smaller bronchi. In none of the cases was there evidence of any lesions of the other viscera.

If the animals were killed early—within the first twelve hours—although no gross changes, or, at most, localized areas of moderate congestion were seen, the streptococci could not only be cultivated from the lung tissue, but they were readily seen with the microscope, after staining by Gram's method, scattered here and there in considerable numbers in the air-vesicles, in the larger air-spaces, and in the bronchioles. They lay in part free in these situations, and in part were clustered about the alveolar epithelium. It was not easy to decide whether the epithelium actually contained the bacteria or whether they simply lay on the surface. I have not been able, even as early as three and a quarter hours after the injection of the streptococci into the trachea, to find any of them in bronchi large enough to be lined with ciliated epithelium.

A microscopical examination was made of the lungs of the rabbits which were either killed or died, at the following intervals after the intratracheal injection of the streptococcus, 3¼, 12, 20, 24, 28, 40, 60 hours, and 3, 4, 8, 10 days. This examination showed in general that in four out of the seven lungs in which no gross lesions were visible, there was actually a considerable amount of lobular inflammation with more or less bronchitis, and that the same condition prevailed in the lungs which showed gross lesions. But in the latter cases the inflammatory lesions were more extensive and were usually associated with congestion, thickening of the walls of the air-vesicles, more or less atelectasis, and swelling of the smaller bronchial lymph nodes.

Cultures were made in the usual way. In no case were streptococci found in the viscera other than the lungs, and after from twelve to twenty-eight hours they were found in every case to have disappeared from the lungs also.

Before twelve hours I have been unable to find any evidence of inflammation save here and there a moderate congestion of the small veins and capillaries of the pulmonary air-spaces. In animals which died or were killed in from twelve to sixty hours after the injection I have failed to find streptococci either by microscopical examination or by cultures.

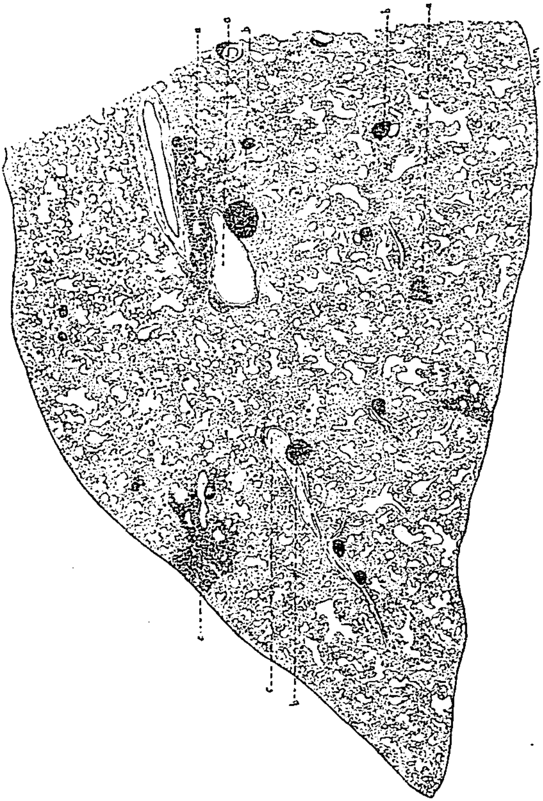
The degree of inflammatory lesion in these animals varies considerably in the different cases. The smaller bronchi may contain pus and the epithelium be loosened and desquamated. The most marked and constant change is the swelling and proliferation of the alveolar epithelium in circumscribed regions. Sometimes only a small cluster of air-vesicles is involved in this way; sometimes the change is to be observed over areas of considerable extent. The air-vesicles are sometimes filled nearly full of new cells, which, from the karyokinetic figures which are to be observed in the nuclei (Plate IV. Fig. 1), I conclude to be derived from the alveolar epithelium. With these larger cells are mingled varying numbers of pus-cells and often a little fibrin (see Plate IV. Fig. 2). The adventitia of the smaller veins in certain regions is apt to be infiltrated with leucocytes (Plate IV. Fig. 1), and the lymph nodules about the smaller bronchi to be much swollen and prominent (Plate III.).

In animals killed after this period—sixty hours—when any lesion at all was found there was apt to be the same kind of exudation in the air-spaces, but the walls of the air-spaces and the smaller bronchi appear thicker than normal, and sometimes with, sometimes without, atelectasis; the lung was dense and firm in patches.

SUMMARY.—It would thus appear that the most common effect of the injection of a moderate amount of the Streptococcus diphtheriæ into the lungs of rabbits through the trachea is to cause a well-marked broncho- and lobular pneumonia with hyperplasia of the lymph nodules; that the bacteria disappear early from the lungs, and the pneumonia in many cases is slight in extent and evanescent; but that in a few cases the inflammation is prolonged by an involvement of the walls of the air-spaces.

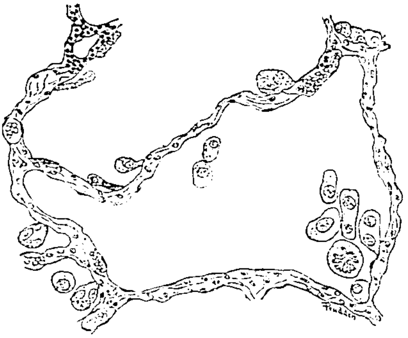
INJECTION OF THE STREPTOCOCCUS DIPHTHERIÆ INTO ANIMALS' LUNGS WHICH WERE ALREADY THE SEAT OF INFLAMMATION.—In order to learn the effects of the streptococcus when introduced into lungs which were already in an inflamed condition, I have induced in another series of animals both mild and severe inflammation of the bronchial mucous membrane by the preliminary introduction of a few drops either of strong or very dilute solutions of ammonia through the trachea. This

PLATE III.



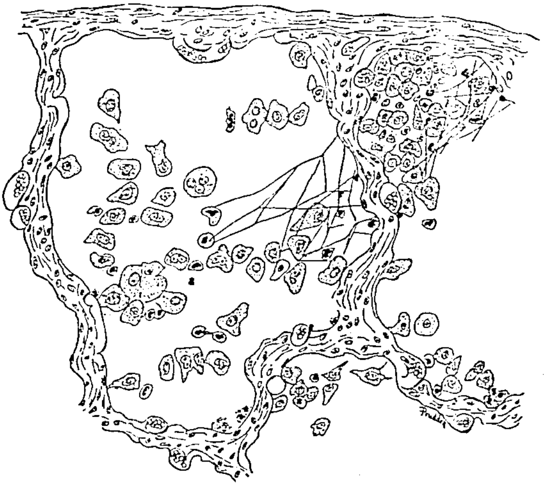
Section from lung of rabbit ten days after injection of the Streptococcus diphtheriæ through the trachea. *a*, areas of lobular pneumonia; *b*, hyperplastic lymph nodules; *c*, bronchi.

PLATE IV.—FIG. 1.



Air vesicles of lung of rabbit dead on third day after tracheal injection of the Streptococcus diphtheriæ. Showing proliferation of alveolar epithelium and collection of leucocytes around a small vein. The bacteria have disappeared.

FIG. 2.



Air vesicles from lung of rabbit dead sixty hours after tracheal injection of the Streptococcus diphtheriæ. The exudation consists of epithelium, leucocytes, and fibrine. The streptococci have disappeared.

was followed at varying intervals by the introduction of two to three c.c. of a beef-tea culture of the streptococcus.

It is difficult in these experiments to decide how much of the broncho-pneumonic lesions which are almost invariably observed when the animals are killed after from twenty-four to twenty-seven hours are due to the ammonia and how much to the streptococci. For the preliminary experiments on ammonia injections alone showed that a broncho-pneumonia very similar in character to that caused by the streptococci alone was almost always induced. The streptococci, of course, formed no part of the exudation in the air-spaces in the cases in which ammonia alone was used. In the animals which had received both ammonia and streptococci, however, the lesions are more marked and extensive, and the bacteria did not disappear so early from the lungs as when the inflammation was induced by them alone.

This fact would seem to furnish another illustration of the well-established principle that certain pathogenic bacteria maintain their existence with greater difficulty in the presence of healthy cells of the living body than when the vitality of the latter is impaired.

COMPARATIVE EXPERIMENTS BY THE INTRODUCTION OF STAPHYLOCOCCUS PYOGENES INTO THE LUNGS.—For the sake of comparison, I have repeated the above detailed experiments on animals, using, instead of the Streptococcus diphtheriæ the Staphylococcus pyogenes aureus. The cultures used were from three of the cases of broncho-pneumonia, and eight animals were injected through the trachea. Four died at from fifteen hours to three days, and in these, as well as in those which showed no signs of illness and which were killed at varying intervals, a moderate amount of lobular pneumonia was found in every case. Cultures and microscopical examinations showed that the staphylococcus was present in diminishing numbers in the affected regions of the lungs up to the third day. After this none could be detected. The general and minute characters of the lesions are similar to those induced by the injection of the streptococcus, save that pus-cells are apt to preponderate in the exudation in the air-spaces. Experiments similar to these with the Staphylococcus pyogenes aureus have been done by Fleck and Laehr (12), who readily succeeded in inducing circumscribed areas of inflammatory consolidation in the lungs of rabbits. They found also that the bacteria, introduced in larger quantities than in my experiments, disappeared in a short time. The appearances which they noted were interpreted as indicating the epithelium and leucocytes in the exudation as the active factors leading to the destruction of the bacteria.

While these experiments with the staphylococcus show that it, as well as the streptococcus, may induce localized inflammation of the lungs, the small number in which they were found in our cases of diphtheritic broncho-pneumonia and the inconstancy of the occurrence would lead us, as above stated, to the opinion that while they may act as complicating agents, they are not the prominent etiological factors in the disease.

It seems not improbable from some preliminary observations which I have made on the broncho- and lobular pneumonia accompanying measles and whooping-cough, that under these conditions the Staphylococcus pyogenes aureus may play an important part in inciting the pulmonary inflammation.

SUMMARY.

We have seen that there is a group of secondary inflammations of the lungs called lobular and broncho-pneumonia, occurring under a great variety of conditions, about the direct inciting cause of which we know very little. Of these we have selected for our studies the lobular and broncho-pneumonia which so frequently complicate diphtheria.

Dr. Northrup has shown by statistical data, derived from the clinical and pathological records of the New York Foundling Asylum and from foreign sources, how frequent and important this complication of diphtheria is.

We have examined morphologically and by cultures the lungs of seventeen children dead of diphtheria complicated by pneumonia. The pseudo-membranes in all but one of these cases had been shown by a previous study to contain a streptococcus, which was, apparently, the cause of the diphtheria. In all but one of the cases of pneumonia the lungs contained a similar streptococcus (it was the same case which was exceptional in both series of studies). We have found no other species of bacteria in these lungs with such frequency and abundance as to justify the belief that it stood in a direct causative relation to the inflammation.

We have been able to induce in rabbits, with the greatest uniformity, by the intratracheal injection of pure cultures of the streptococcus isolated from the children's lungs a lobular and broncho-pneumonia very similar in its character to that with which we started in the children. We have found that the injected bacteria do not, as a rule, gain access, at least in demonstrable numbers, to the blood and the other viscera of the animals.

Though we have no detailed observations to record bearing upon the theory of phagocytosis, we have learned that after inciting the local inflammatory process in the lungs of the animals the bacteria rapidly disappear. This observation seems to explain why, in children's lungs which are the seat of broncho-pneumonia consecutive to diphtheria, we often find the streptococci in large numbers in some of the inflammatory foci, while in others they are few in number or entirely absent.

We arrive, finally, at the conclusion that the acute lobular and broncho-pneumonia which is apt to complicate diphtheria in the upper air-passages in children, is, at any rate in the set of cases which we have examined, a form of inspiration pneumonia, induced by the Streptococcus diphtheriæ which finds access to the lungs from the foci of diphtheritic inflammation in the air-passages above.

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A CASE OF NEPHRO-URETERO-LITHOTOMY,

WITH REMARKS UPON THE ANATOMY OF THE PELVIS OF THE KIDNEY.

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MRS. M., of Beverly, whose case forms the subject of this paper, began to suffer from pyelitis some time in 1883 or 1884, when she was about forty-three years old. From the beginning up to the time of operation, pus was present in the urine, in varying amount, but never absent; and occasionally there was albumin in small amount; almost always oxalate of lime, and very frequently uric acid crystals. There were no attacks of renal colic, never any very severe pain, but always a dull aching discomfort in the lumbar region. The only medicine that alleviated the trouble much was lithiated hydrangea, which distinctly lessened the amount of pus, and gave some relief to the lumbar aching.

On January 2, 1888, after not having seen the patient for several months, I was called to attend her in an attack of acute bronchial catarrh, mainly affecting the left lung and accompanied by very distressing dyspnœa. Under treatment she was relieved in two days of her harassing cough and extreme difficulty of breathing, when she began to